

What is claimed is:

1. A method of determining disease status of a patient suffering from a disease characterized by aberrant expression of one or more cell surface receptor complexes, the method comprising the steps of:
 - measuring directly in a patient sample an amount of each of one or more cell surface receptor complexes;
 - comparing each such amount to its corresponding amount in a reference sample; and
 - correlating differences in the amounts from the patient sample and the respective corresponding amounts from the reference sample to the disease status the patient.
2. The method of claim 1 wherein said patient sample is a fixed tissue sample or a frozen tissue sample.
3. The method of claim 2 wherein said one or more cell surface receptor complexes are one or more receptor tyrosine kinase complexes and wherein said disease is a cancer.
4. The method of claim 1 wherein said one or more cell surface receptor complexes are one or more PDGF receptor complexes.
5. The method of claim 4 wherein said one or more PDGF receptor complexes are selected from the group consisting of PDGFR α homodimers, PDGFR β homodimers, PDGFR α -PDGFR β heterodimers, PDGFR-SHC complexes, PDGFR-PI3K complexes, Her1-PDGFR receptor dimers, Her2-PDGFR receptor dimers, Her3-PDGFR receptor dimers, and PDGFR-IGF-1R receptor dimers.
6. The method according to claims 4 or 5 wherein said disease is cancer or wherein said disease is associated with an aberrant fibrotic condition.
7. The method of claim 6 wherein said cancer is selected from the group consisting of breast cancer, ovarian cancer, and glioblastoma.
8. The method of claim 7 wherein said one or more PDGF receptor complexes are determined by the steps of:
 - providing for each of said one or more PDGF receptor complexes a reagent pair comprising a cleaving probe having a cleavage-inducing moiety with an effective proximity, and

one or more binding compounds each having one or more molecular tags attached thereto by a cleavable linkage, the molecular tags of different binding compounds having different separation characteristics;

5 mixing the cleaving probe and the one or more binding compounds for each of said one or more PDGF receptor complexes with said patient sample such that the cleaving probe and the one or more binding compounds specifically bind to their respective PDGF receptor complexes and the cleavable linkages of the one or more binding compounds are within the effective proximity of the cleavage-inducing moiety so that molecular tags are released; and
10 separating and identifying the released molecular tags to determine the presence or absence or the amount of said one or more PDGF receptor complexes in said patient sample.

9. The method of claim 1 wherein said one or more cell surface receptor complexes are one or more VEGF receptor complexes.

15 10. The method of claim 9 wherein said one or more VEGF receptor complexes are selected from the group consisting of VEGFR1 homodimers, VEGFR2 homodimers, VEGFR1-VEGFR2 heterodimers, VEGFR2-VEGFR3 heterodimers, VEGFR2-SHC complexes, and VEGFR3-SHC complexes.

20 11. The method according to claims 9 or 10 wherein said disease is cancer or wherein said disease is associated with aberrant angiogenesis.

12. The method of claim 11 wherein said one or more VEGF receptor complexes are determined by the steps of:

25 providing for each of said one or more VEGF receptor complexes a reagent pair comprising a cleaving probe having a cleavage-inducing moiety with an effective proximity, and one or more binding compounds each having one or more molecular tags attached thereto by a cleavable linkage, the molecular tags of different binding compounds having different separation characteristics;

30 mixing the cleaving probe and the one or more binding compounds for each of said one or more VEGF receptor complexes with said patient sample such that the cleaving probe and the one or more binding compounds specifically bind to their respective VEGF receptor complexes and the cleavable linkages of the one or more binding compounds are within the effective proximity of the cleavage-inducing moiety so that molecular tags are released; and

35 separating and identifying the released molecular tags to determine the presence or absence or the amount of said one or more VEGF receptor complexes in said patient sample.

13. The method of claim 1 wherein said one or more cell surface receptor complexes are receptor dimers selected from the group consisting of VEGFR1(Flt1)-VEGFR2(KDR), VEGFR2(KDR)-VEGFR2(KDR), PDGFR α -PDGFR α , PDGFR α -PDGFR β , PDGFR β -PDGFR β ,
5 Kit/SCFR homodimers, an FGFR dimer, NGFR(TrkA)-NGFR(TrkA), α_2 -adrenergic receptor homodimer, α_2 -adrenergic- β_2 -adrenergic receptor heterodimer, β_2 -adrenergic receptor homodimer, GABA $_B$ R1-GABA $_B$ R2 receptor heterodimer, ATII receptor homodimer, cholecystokinin-dopamine receptor heterodimer, bradykinin B2 receptor homodimer, M2-M3 muscarinic receptor heterodimer, CCR2 receptor homodimer, μ - δ opioid receptor heterodimer,
10 D1 dopamine receptor homodimer, 5-HT 1B-5-HT 1D receptor heterodimer, D2 dopamine receptor homodimer, α_{2c} -adrenergic-M3 muscarinic receptor heterodimer, D3 dopamine receptor homodimer, and β_2 -adrenergic- δ opioid receptor heterodimer.

14. The method of claim 13 wherein said one or more receptor dimers are determined by the
15 steps of:

providing for each of said one or more receptor dimers a reagent pair comprising a cleaving probe having a cleavage-inducing moiety with an effective proximity, and one or more binding compounds each having one or more molecular tags attached thereto by a cleavable linkage, the molecular tags of different binding compounds having different separation
20 characteristics;

mixing the cleaving probe and the one or more binding compounds for each of said one or more receptor dimers with said patient sample such that the cleaving probe and the one or more binding compounds specifically bind to their respective receptor dimers and the cleavable linkages of the one or more binding compounds are within the effective proximity of the
25 cleavage-inducing moiety so that molecular tags are released; and

separating and identifying the released molecular tags to determine the presence or absence or the amount of said one or more receptor dimers in said patient sample.

15. A method of selecting a patient for treatment of a cancer with one or more dimer-acting
30 drugs, the method comprising the steps of:

isolating a patient sample containing cancer cells from a patient;

measuring directly in the patient sample an amount of each of one or more cell surface receptor dimers;

comparing each such amount to its corresponding amount from a reference sample; and

selecting the patient for treatment with one or more dimer-acting drugs whenever an amount of one or more cell surface receptor dimers from the patient sample exceeds the respective corresponding amount from the reference sample.

5 16. The method of claim 15 wherein said cell surface receptor dimer is a VEGFR dimer and said dimer-acting drug is selected from the group consisting of PTK787/K222584, ZD6474, SU6668, SU11248, CHR200131, CP547632, AG13736, CEP7055/5214, and KRN633.

17. The method of claim 15 wherein said cell surface receptor dimer is a PDGFR dimer and
10 said dimer-acting drug is selected from the group consisting of SU6668, SU11248, AG13736, CHR200131.

18. The method of claim 15 wherein said cell surface receptor dimer is an FGFR dimer and said dimer-acting drug is selected from the group consisting of CP547632 and CHR200131.

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19. The method according to claims 15, 16, 17, or 18 wherein aid one or more cell surface receptor dimers are determined by the steps of:

providing for each of said one or more cell surface receptor dimers a reagent pair comprising a cleaving probe having a cleavage-inducing moiety with an effective proximity, and
20 one or more binding compounds each having one or more molecular tags attached thereto by a cleavable linkage, the molecular tags of different binding compounds having different separation characteristics;

mixing the cleaving probe and the one or more binding compounds for each of said one or more cell surface receptor dimers with said patient sample such that the cleaving probe and the
25 one or more binding compounds specifically bind to their respective cell surface receptor dimers and the cleavable linkages of the one or more binding compounds are within the effective proximity of the cleavage-inducing moiety so that molecular tags are released; and

separating and identifying the released molecular tags to determine the presence or absence or the amount of said one or more cell surface receptor dimers in said fixed tissue
30 sample.

20. The method of claim 19 wherein said patient sample is a fixed tissue sample, a frozen tissue sample, or circulating epithelial cells.

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21. A method of determining disease status of a patient suffering from a disease characterized by aberrant expression of one or more cell surface receptor complexes, the method comprising the steps of:
- 5 measuring directly in a patient sample an amount of each of one or more cell surface receptor complexes;
- comparing each such amount to its corresponding amount in a reference sample;
- correlating differences in the amounts from the patient sample and the respective
- 10 corresponding amounts from the reference sample to the disease status the patient; and
- wherein each of said one or more cell surface receptor complexes are determined by the steps of:
- providing for each of said one or more cell surface receptor complexes and one or more tissue indicators a reagent pair comprising a cleaving probe having a cleavage-inducing moiety
- 15 with an effective proximity, and one or more binding compounds each having one or more molecular tags attached thereto by a cleavable linkage, the molecular tags of different binding compounds having different separation characteristics;
- mixing the cleaving probe and the one or more binding compounds for each of said one or more cell surface receptor complexes and one or more tissue indicators with said patient
- 20 sample such that the cleaving probe and the one or more binding compounds specifically bind to their respective targets and the cleavable linkages of the one or more binding compounds are within the effective proximity of the cleavage-inducing moiety so that molecular tags are released; and
- separating and identifying the released molecular tags to determine the presence or
- 25 absence or the amount of said one or more cell surface receptor complexes in said patient sample.
22. The method of claim 21 wherein said disease is a cancer and wherein said patient sample is a fixed tissue sample, a frozen tissue sample, or circulating epithelial cells.
- 30 23. The method of claim 22 wherein said disease status is responsiveness of said patient to treatment with a dimer-acting drug.
24. The method of claim 22 wherein said cancer is selected from the group consisting of breast cancer, ovarian cancer, prostate cancer, and colorectal cancer.

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25. The method of claim 22 wherein said one or more cell surface receptor complexes are selected from the group consisting of PDGFR α homodimers, PDGFR β homodimers, PDGFR α -PDGFR β heterodimers, PDGFR-SHC complexes, PDGFR-PI3K complexes, Her1-PDGFR receptor dimers, Her2-PDGFR receptor dimers, Her3-PDGFR receptor dimers, PDGFR-IGF-1R receptor dimers, VEGFR1 homodimers, VEGFR2 homodimers, VEGFR1-VEGFR2 heterodimers, VEGFR2-VEGFR3 heterodimers, VEGFR2-SHC complexes, and VEGFR3-SHC complexes.

26. The method according to claims 21, 22, 23, 24, or 25 wherein said tissue indicators are tubulin or cytokeratin.

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